Nosocomial transmission of NDM-1-producing *Escherichia coli* within a non-endemic area in France

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Abstract

Two patients with no travel history and sharing the same room were colonized by the same strain of New Delhi metallo-β-lactamase 1 (NDM-1)-producing *Escherichia coli* within a geographical area not endemic for this highly multidrug-resistant bacterium. It was documented an absence of an epidemiological and bacteriological link with a third patient returning from India after surgery and found to be infected by an NDM-1-producing *Citrobacter* strain during the same period. Despite extensive investigation, the source of contamination of the two former patients was not elucidated. This case report illustrates the need of investigating rapidly the emergence of highly multidrug-resistant *Enterobacteriaceae*, to stop their dissemination in a nosocomial setting.

Keywords: Carbapenemase, cross-transmission, multidrug-resistant bacterium, NDM1-producing *Escherichia coli*, nosocomial

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Enterobacteriaccae producing New Delhi metallo-β-lactamase 1 (NDM-1) were shown recently to be an emerging problem in public health [1,2]. Many cases have been reported worldwide, including in European countries with no close links with Asia [3].

An 86-year-old man (patient 1) was hospitalized for a hip fracture in June 2010, and again for anaemia requiring blood transfusions in July 2010 at the university hospital of Saint-Etienne, France. Because of catheter-associated urinary tract infection, four urinary samples were cultured (Fig. 1); the last two specimens showed successively *Enterococcus faecalis* and *Escherichia coli*, both of which exhibited a sensitive pattern with current antimicrobial agents. These two infections were treated, respectively, with amoxycillin and fluoroquinolone. The patient was then discharged to a rehabilitation facility 25 km from the first setting. In October 2010, before being transferred to a long-term-care facility, he was found to be colonized in urine and stools by a strain of *E. coli* resistant to many antimicrobial drugs, including aminoglycosides, fluoroquinolones, trimethoprim–sulphamethoxazole, penicillins, cephalosporins, and carbapenems. The MICs of imipenem, ertapenem, meropenem and doripenem interpreted according to CLSI guidelines [4] were 4, 4, 1 and 1.5 mg/L, respectively. The strain was sensitive to colistin and tigecyclin (MIC of 0.5 mg/L for both drugs). With PCR techniques specific for β-lactam resistance genes, this strain tested positive for three β-lactamase genes (TEM-1, OXA-10, and CMY-16) and for the NDM-1 gene [5].

In the course of the epidemiological investigation related to the discovery of this case of colonization involving an NDM-1-positive bacterium, an 85-year-old patient sharing the same room (patient 2) was found to be colonized at the intestinal level by a similar *E. coli* strain, in terms of both antibiotic resistance and genotypic pattern by rep-PCR-based fingerprinting with Diversilab (bioMérieux, Marcy l'étoile, France). This patient had been previously hospitalized in September and October 2010 in the neurosurgery unit of the university hospital of Saint-Etienne (Fig. 1).

With a follow-up of 7 months, patient 1 was found to be chronically contaminated at both the intestinal and urinary tract levels; by contrast, patient 2 tested negative 3 months later. Both patients denied any travel outside France during the last 5 years.

Within the same period (August 2010), an 18-year-old female (patient 3) repatriated from Pondicherry, India was found to be infected with a multiresistant strain of *Citrobacter freundii* harbouring the NDM-1 gene [6]. The infection was limited to the urinary tract, and ceased after the removal of the urinary catheter. No intestinal colonization was observed, despite an exhaustive screening including 15 successive samplings during the next 3 months (Fig. 1).

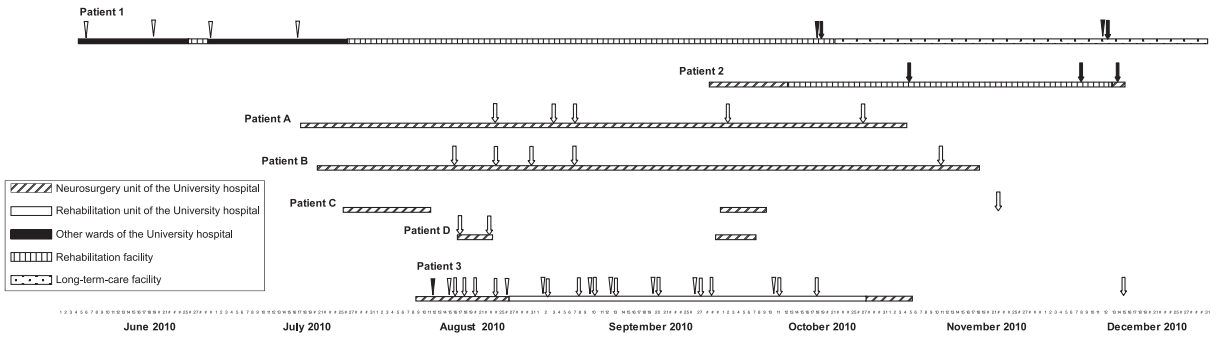

FIG. 1. Temporal diagram of cases harbouring NDM-1-producing bacteria (patients 1–3) and contacts (patients A–D) according to their hospital location(s). Arrows and tips represent the times of stool and urine samplings, respectively; plain symbols correspond to samples found to be positive for an NDM-1-producing bacterium.

In order to address the potential relationship between these episodes, a large epidemiological investigation was performed, notably because patients 2 and 3 had been hospitalized in the same neurosurgery ward within a 2-month period, despite a gap of 5 weeks between the two stays (Fig. 1). As shown in Table 1, patients sharing the same healthcare team were divided into two groups according to the time of implementation of hygienic contact precaution measures. From a total of 269 presumed contact patients, 195 (72.5%) could be sampled by rectal swabbing, as recommended by recent French guidelines [7]. With the exception of the cross-transmission described above in the rehabilitation facility (cases 1 and 2 in Table 1), no secondary case was detected. Fig. 1 reports the temporal course of the three cases with NDM-1-positive strains of *Enterobacteriaceae* and of four other patients (A–D) who could have constituted an epidemiological link between patients 2 and 3 in the neurosurgery ward, because they had been present in this ward either for a long period of time (patients A and B) or for two successive stays matching those of patients 1 and 3 (patients C and D), despite no documented contact with the index cases. These four patients tested negative for NDM-1-positive isolates in rectal swabs (Fig. 1). In addition, a cross-sectional investigation consisting of rectal swabbing of all patients present in the neurosurgery ward was performed on the 9 November 2010; it identified no further case of colonization. The spouses of patients 1 and 2 who received chronic care in other facilities (haemodialysis and long-term-care units, respectively) also screened negative for NDM-1-producing isolates by rectal swabbing.

From a bacteriological point of view, additional experiments, with the Kieser method [8] and a PCR-based replicon typing method [9], were conducted to type the NDM-1 plasmids in *E. coli* and *C. freundii* strains. The *E. coli* strains were found to harbour a 150-kb plasmid, belonging to Inc type A/C and carrying the associated resistant determinants OXA-10 and CMY-16. By contrast, the *C. freundii* strain harboured a 65-kb plasmid (pSTE-1) that was found to be untypeable in the Inc classification [6].

This case report illustrates the ability of multidrug-resistant NDM-1-producing *E. coli* strains to spread in patients sharing the same environment. A few cases of cross-transmission of multidrug-resistant NDM-1-producing *Enterobacteriaceae* strains have been published previously [3]. To the

TABLE 1. Epidemiological investigation performed in contact patients of the three cases found to be infected or colonized by an NDM-1-producing bacterium; all of the patients tested negative at least once by rectal swabbing for the presence of bacteria harbouring the NDM-1 gene

		Patients sharing the same healthcare team					
		Before implantation of contact precaution measures			After implantation of contact precaution measures		
Case no.	Ward and facility	Total	Tested	Sample mean per patient	Total	Tested	Sample mean per patient
1	Rehabilitation facility	47	43	2.3	–	–	–
2	Neurosurgery unit	75	32	1.5	–	–	–
	Rehabilitation facility	42	40	2.1	–	–	–
3	Neurosurgery unit	55	42	1.7	30	27	1.8
	Rehabilitation unit[a]	14	5	1.0	6	6	3.0

[a]The rehabilitation unit of the university hospital is a different place from the rehabilitation facility.

best of our knowledge, our case report is the second one to document nosocomial transmission of an NDM-1 gene involving an *E. coli* strain. The first one, published very recently, concerned a cluster of septicaemic newborns with possible transfer of NDM-1 genes from imipenem-resistant Gram-negative bacilli to imipenem-susceptible *E. coli* [10]. These observations deserve special attention, because, in contrast to other *Enterobacteriaceae*, *E. coli* is a constant inhabitant of the human digestive tract; they suggest that such highly multidrug-resistant strains should be rapidly investigated to stop their dissemination in a nosocomial setting.

A further peculiarity of this episode is that it occurred concomitantly with another case of infection caused by an NDM-1-producing bacterium in the more usual context of repatriation from India [1,11]. Despite the simultaneity of these cases in a same area at the same time, extensive bacteriological (different plasmids) and epidemiological investigations (Table 1) formally excluded a common origin. The source of contamination of patients 1 and 2 remains unknown. External sources, such as endoscopes or contact with medical students who had worked in Asian hospitals during holidays, were excluded (data not shown). A possible explanation lies in the digestive colonization of a healthcare worker who had travelled abroad. In fact, the colonization by NDM-1-producing strains of healthy people returning from Asia with [12] or without [13] stay in healthcare settings has been previously reported. As multiple units had harboured the two patients, a systematic screening at the digestive level of healthcare workers was difficult to perform, especially because this measure is not recommended by current French guidelines [7]. Previous reports have documented the autochthonous acquisition of NDM-1-producing *Enterobacteriaceae*, including *Morganella morganii* and *Providencia rettgeri* [14] and *Klebsiella pneumoniae* [15], in patients with no history of travel in areas known to be endemic for NDM-1-producing strains. As in our cases, the source of contamination of these three patients remained unknown.

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Transparency Declaration

All authors declare no conflicts of interest.

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